Amendments to the Title

Please amend the title as follows:

"~~METHOD~~ METHODS FOR MEASURING ~~SUBSTANCE~~ SUBSTANCES HAVING AFFINITY"

Amendments to the Specification

Please replace the paragraphs at page 4, lines 10-22 with the following amended paragraph:

The present inventors intensively studied means for measuring agglutinates of carrier particles to resolve the problems described above. As a result, the inventors discovered that measurement accuracy is improved by counting particles or agglutinates using three-dimensional information as an indicator, thereby completing the present invention. Specifically, the present invention relates to the following measurement methods and devices:
[1] a method for measuring an affinity substance, which comprises the steps of:
(1) mixing carrier particles with an affinity substance to be measured and applying a voltage pulse to supply an electric field, wherein the carrier particles are bound to a binding partner having an activity to bind to the affinity substance; or
(1') mixing carrier particles with an agglutination reagent component and an affinity substance to be measured, and applying a voltage pulse to supply an electric field, wherein the carrier particles are bound to a binding partner having an activity to bind to the affinity substance, and wherein the affinity substance inhibits agglutination of the carrier particles caused by the agglutination reagent;

Please replace the paragraph at page 6, line 34 through page 7, line 9 with the following amended paragraph:

Either an antigenic substance or an antibody recognizing the substance may be used as the affinity substance and the other as the binding partner. Herein, the affinity substance refers to a target substance to be measured. On the other hand, the binding partner refers to a substance that can be used as a probe to measure the affinity substance and has an activity to bind to the affinity substance. Thus, an antibody can be used as the binding partner when an antigen is measured. Conversely, an antibody recognizing an antigen can be used as the binding partner in the measurement of the antibody. For example, any antibody that can be measured based on an immunological agglutination reaction using latex or blood cell as a carrier can be used as an affinity substance of the present invention. Antibodies against HBs (surface antigen of hepatitis B virus), HBc (core antigen of hepatitis B virus), HCV (hepatitis C virus), HIV (AIDS virus), TP (syphilis), and such have been measured using immunological agglutination reactions.

Please replace the paragraph at page 10, lines 15-28 with the following amended paragraph:

Herein, the voltage pulse typically refers to ~~a voltage having a wave or waveform whose amplitude undergoes transitions from a steady state to a particular level, maintains the level for a finite time, and then returns to the original state~~ a voltage that has a wave or waveform, in which the voltage undergoes transitions from a steady state to a particular level, maintains that level for a finite time, and then returns to the original state. Alternating voltage is representative of such a voltage pulse. Alternating voltage is a periodic function of time with an average voltage value of zero. Alternating voltages include sine wave, rectangular wave, square wave, and sawtooth wave voltages, which have obvious periodic amplitudes. In general, the positive electric potential and the negative electric potential in an arbitrary cycle of alternating voltage have equal areas, making the sum of the two zero. Each area is defined by the curve above or below the horizontal axis, where the electric potential difference is zero. In the present invention, voltage pulses are applied to prevent electrolysis of reaction solutions. Accordingly, when electrolysis does not take place in a reaction solution, or if the electrophoresis, when actually occurs, can be suppressed to an extent that does not substantially interfere with the reaction, voltage pulses having a non-zero sum of positive and negative electric potentials may be applied.

Please replace the paragraph at page 28, line 33 through page 29, line 7 with the following amended paragraph:

To 1 ml of glycine buffer (50 mM glycine, 50 mM sodium chloride, and 0.09% NaN3; hereinafter abbreviated as "GBS") ~~1.0 mL~~ containing 0.1 mg of an anti-human CEA antibody (Dako), 1 ml GBS suspension of 1.0% 2-μm latex (Polysciences Inc.) was added. After 2 hours of incubation at 37°C, the suspension of sensitized latex was centrifuged (at 10000 rpm for 15 minutes), and the resulting supernatant was discarded. The precipitate was suspended in GBS containing 2% bovine serum albumin. After 1 hour of incubation at 37°C, the suspension was again centrifuged (10000 rpm, 10 minutes), and the resulting supernatant was discarded. The precipitate was suspended in GBS (pH 8.2) containing 0.2% bovine serum albumin, 10% sucrose, and 5% choline chloride to prepare an anti-human CEA antibody-sensitized latex reagent (latex concentration was 1% W/V; 2-μm reagent). A 3-μm reagent was prepared using 3-μm latex (Polysciences Inc.) by the same procedure described above.

Please replace the paragraph at page 33, lines 13-19 with the following amended paragraph:

Equal amounts of each sample and the reagent prepared in Example [[5]] 4 were added to a test tube, and the resulting mixtures were incubated at 37°C for 20 minutes. 0.5 μl of the reaction solution was diluted with 20 ml of physiological saline. Likewise, the agglutination rate was determined using the diluted solution, by measuring the particle size distribution of latex particles with a Coulter counter by the same procedure described in Example [[5]] 4. The measurement was repeated five times by the same procedure described in Example [[5]] 4. The results are shown in Tables 4 and 5, and Fig. 9.

Please replace the paragraph at page 34, line 12 through page 35, line 1 with the following amended paragraph:

The detection limit of the methods of the present invention can be estimated to be 0.015 ng/ml (Fig. 8) from comparing the detection limits in Figures 8 and 9. Meanwhile, the detection sensitivity in the conventional method is 1.9 ng/ml (Fig. 9). Thus, the sensitivity of the present invention is more than 100 times higher. In addition, the reproducibility of the present invention at each antigen concentration is also superior, and the ~~CV~~ coefficient of variation (CV) value is roughly in the range of 1 to 2% (the simultaneous reproducibility at an antigen concentration of 1.95 ng/ml is 1.33% CV for the present invention and 9.86% for the conventional method). Excellent linearity is seen up to an antigen concentration of 500 ng/ml. These findings show that when compared to the conventional method, measurements by the present invention, which accelerates reactions through pearl chain formation by applying voltage pulses, can be achieved in a very short time at high sensitivity with excellent reproducibility and linearity.